Study of Associated Risk Factors of Autism Spectrum Disorder in Upper Egyptian Children

*Hosny Mohammed Ahmed El-Masry, Mohammed Abo-Alwafa Aladawy, Rana Atef Said Gbr **

Corresponding Author: Rana Atef Said Gbr *E-Mail:* **ranagbr9@gmail.com**

** Department of Pediatrics, Faculty of Medicine, Al-Azhar University (Assiut), Egypt*

ABSTRACT:

Background: Autism spectrum disorder (ASD) is a neurological and developmental disorder that affects how people interact with others, communicate, learn, and behave. Hunderd of autism risk genes and various social factors have been discovered.

Aim of the Work: To evaluate various perinatal and environmental risk factors associated with autism spectrum disorder.

Methods: The current study included 20 children diagnosed as autism spectrum disorder according to DSM-5 (Diagnostic and Statistical Manual of Mental disorders Fifth Edition), aged from 2 years to 12 years (12 male and 8 females). All children were subjected to a detailed history taking and thorough clinical examination with special emphasis on neurological examination and their clinical and social risk factors. Assessment of severity of autistic symptoms was done using childhood autism rating scale (CARS), intelligence quotient (IQ) was evaluated by use of Stanford Binet Intelligence Scale, 4th edition (SB4).

Results: 60% of the studied patients were males. The mean +_SD of age was 7.43+_3.23. current study have shown that low socioeconomic status (85%) is significantly associated with ASD. Family history of autism was 25%. CARS assessment revealed that 55% of patients were mild to moderate autism and 45% were with severe autism. IQ with wide range from mild to severe mental retardation, 25% mildly defective, 40% moderately defective and 35% severely defective. 45% of parents were consanguineous. 35% of the cases came from urban areas and 65% from rural. Advanced maternal age more than 35 years in 5% of children and 15% of mothers were educated 85% were uneducated. As regard to pregnancy complications, there was no history of maternal infection, no maternal bleeding or preeclampsia and DM, none of the studied mothers reported history of exposure to chemical radiation during pregnancy. All of the children in the study were full term. 60% of the cases delivered by cesarean delivery and 40% were delivered by vaginal delivery. 5% of cases reported prolonged labor and 10% of the cases reported history of hypoxia but there is no history birth trauma. 5% of cases needed resuscitation after delivery and 15% needed NICU admission. 5% of cases reported neonatal jaundice. The type of feeding was breast feeding in 50% of cases and 50% were bottle feeding. Stereotyped movements, language, social impairment and social risk factors were presented in all autistic children (N=20). 95% exposed to media (TV or mobile) more than 2 hours daily while 75% were social deprived.

Conclusions: The most common risk factors among the patients in the current study sample was the social factors which associated with high incidence of autism , social deprivation and increase time exposed to media, in correlation with low social and economic level and low educational level of patients' mothers.

Keywords: Autistic spectrum disorder ASD, Children, Risk factors, Upper Egypt.

Introduction:

Autistic spectrum disorder (ASD) is known as a neurodevelopmental disorder that affects how people interact, communicate, learn and behave with others, typically manifests in early childhood by age of 2 or 3 years as impaired social communication and restricted, repetitive, stereotyped patterns of behaviors, interests or activities and falls on and inability to function effectively in school, work, and other areas of life a spectrum ranging from mild to severe caused by differences in the brain including autistic disorder, pervasive developmental disorder and Asperger syndrome **(American Psychiatric Association; 2013).**

The Centers for Disease Control and Prevention (CDC) reports that autism affects 1 in 36 children. Also ASD more common in males. In the U.S., about 4 in 100 boys and 1 in 100 girls have autism Boys are nearly 4 times more likely to be diagnosed with autism than girls **(Center of Disease Control and Prevention, 2023).**

In a recent Egyptian study of Metwally et al. which aimed to provide a national estimate of the prevalence of the high risk of ASD and their determinants. A national screening survey was conducted for 41,640 Egyptian children aged 1 to 12 years. The overall prevalence of children at high risk of ASD was 3.3% (95% CI:3.1%-3.5%). Children living without mothers in homes, suffered from convulsions (AOR = 3.67; 95% * CI / 2.8 - 4.8) a history of cyanosis after birth

(AOR = 1.87 ; 95% CI:1.35-2.59) or history of LBW babies (AOR = 1.53 , 95% CI:1.23-1.89) carried higher odds of being at high risk of ASD **(Metwally et al., 2023).**

Despite the rising prevalence of ASD, a comprehensive understanding of the various factors associated with the condition remains elusive And while previous research has examined perinatal factors in the context of Autism Spectrum Disorder (ASD), Studies focusing on sociocultural factors is limited **(Phone M. et al., 2025).**

Previous studies have determined some risk factors in ASD children such as advanced maternal and paternal age, gestational diabetes, uterine bleeding, type of delivery, low birth weight; low Apgar scores, hyper bilirubinemia, and postpartum hemorrhage have been consistently identified as significant risk factors for ASD. Previous Studies focused on Factors such as advanced maternal and paternal age, gestational diabetes, uterine bleeding, type of delivery, low birth weight; low Apgar scores, hyper bilirubinemia, and postpartum hemorrhaged have been consistently identified as significant risk factors for ASD **(Phone M. et al., 2025).**

The exact cause of ASD is not yet known, but many factors have been related to increased risk for ASD including environmental, biologic, and genetic factors which affect the developing brain as some children seem normal before age 1 or 2 years then suddenly lose language or social skills they already had **(Pinto D, et al ;2010).**

Previous systematic reviews and meta-analyses of environmental risk factors for autism identified environmental risk factors for autism as advanced parental age **(Wu et al., 2017)** and birth trauma, particularly if due to proxies of hypoxia **(Modabbernia et al., 2017).** Moreover, maternal obesity, a short interval between pregnancies, gestational diabetes mellitus and valproate use during pregnancy have all been associated with increased risk of autism. However, it should be noted that these factors cannot be considered causal, but could be reactive, independent or contributory for autism. Studies evaluating risk factors for autism that have reported an absence of association are equally, if not more, important to note, including clear evidence that autism is not associated with vaccination **(Taylor et al., 2014).** Other negative associations include prolonged labour, delivery by caesarean section or assisted vaginal delivery, premature rupture of membranes and the use of assisted reproductive technologies, among other factors. Environmental risk factors could trigger the risk of autism through several complex underlying mechanisms such as genetic and epigenetic effects, inflammation and oxidative stress, or hypoxic and ischemic damage **(Modabbernia et al., 2017).**

Treatment for ASD involves interventions aimed at improving children's adaptive skills and at symptom reduction. There are many types of treatments available may involve more than one approach: Behavioral, Developmental, Educational, Social-Relational, Pharmacological, Psychological, Complementary and Alternative **(Hyman, S.L et al., 2020).**

Therefore, the current study evaluate risk factors associated with autism spectrum disorder, including clinical risk factors for the autistic patients studied and their social risk factors. The current study provides a deeper understanding of the interaction between clinical and social risk factors, contributing to the development of effective support for early diagnosis and subsequent interventions, enabling children to make the best start in life and develop their abilities.

Ethical consideration:

1. Our study was approved by the ethical committee of Faculty of Medicine, Al-Azhar University, Assiut, and conducted in accordance with Helsinki standards 2013.
2. An informed consent was obtained from all parents and participating children.
3. The results and data of the study are confidential, and the patient has the right to keep it.
4. The authors received no financial support for this study, authorship, and/or publication it.
5. No conflict of interest regarding study or publications.

Sample size:

We based the sample size in our study on the previously estimated ASD prevalence in Upper Egypt; A study by **(Metwally AM, et al 2023)** evaluated 41,640 children, estimating ASD prevalence at 1.1% (455 cases). Statistically significant differences in ASD prevalence were observed between Egyptian governorates. With a margin of error set at 0.0049, a confidence level of 95%, and a minimum reliability of 80% for the least reliable questionnaire used in ASD

detection; we chose 20 cases diagnosed with ASD to survey risk factors in Upper Egypt.
This study is a cross-section study includes 20 patients with ASD according to diagnostic and statistical manual of mental health 5th edition (DSM5) criteria, recruited from pediatric neurology outpatient clinic of Al-Azhar university Assiut from 1st of November 2023 to 31th of April 2024.

***Inclusion criteria:**

- Male and female patients with ASD having achieved diagnostic criteria for ASD according to DSM-5 criteria, age range from 2-12 years of life.

***Exclusion criteria:**

- Children with ASD less than 2 or more than12 years of life.
- Children with hearing impairment.
- Children with cerebral palsy.
- Children with congenital brain malformations.

All children included in the current study sample submitted to the following:

I. History and examination:

Detailed history taking, include name, age, sex. Information regarding socio-demographic data, history of maternal exposure to air pollution or insecticide, prenatal and post-natal history: history of maternal protective value as multivitamins intake in early pregnancy (folic acid, vit. D) , history of maternal diseases and drug intake (Antiepileptic drugs like valproic acid, opioids, cocaine, acetaminophen, asthma medications, pain killers, antidepressant drugs), mode of delivery (vaginal, cesarean section, instrumental), labor (prolonged, obstructed, abnormal presentation), risk factors of prematurity, history of neonatal jaundice and anemia), presence of meconium, risk factors of infections (maternal infections viral infections during 1st trimester of pregnancy like influenza, rubella and herpes, bacterial infections during 2nd trimester like yeast infections, respiratory illnesses). Developmental history including mental, language, social and motor development.

Family history of any similar condition and other psychological or mental disorders in the family.

History of early media exposure (age and time of exposure) and history of social deprivation.

II. Clinical examination: with special emphasis on neurological examination. Which includes:

Complete clinical examination including: general examination, systematic: abdominal, chest and neurological examination.

III. Psychometric Assessment: Assessment of severity of autistic symptoms was done using childhood autism rating scale (CARS). Intelligence quotient (IQ) was evaluated by use of Stanford Binet intelligence scale. 4th edition (SB4).

Childhood Autism Rating Scale – Second Edition (CARS™-2) is to help identify the presence of autism in children and to determine the severity of symptoms. It is an individually administered, behavioral rating scale that is completed by someone who knows the child well. Fifteen functional domains are rated on a 4-point scale. Based on informant or clinician observation, the clinician assigns ratings in each domain related to frequency, peculiarity, intensity, and duration **(Schopler et al, 2011)**

Each item is scored on a scale ranging from one to four; higher scores are associated with a higher level of impairment. Total scores can range from a low of 15 (within normal limits on all items) to a high of 60 (severely abnormal on all items). Scores below 30 indicate that the individual is in the non-autistic range, scores between 30 and 36.5 indicate mild to moderate autism, and scores from 37 to 60 indicate severe autism **(Schopler et al, 1980).** In 2010, Schopler and colleagues released the CARS, Second Edition. (CARS2), which includes updated formatting to enhance its ease of use. Separate forms were created based on a person's developmental level.

The CARS-2 has two versions: the standard form, CARS-2-ST, for individuals less than 6 years of age and those with communication difficulties or below average estimated IQs ; and the CARS-2-HF for those 6 years and over who are verbally fluent and have IQ scores over 80.

Method of Administration: 15-item rating scales completed by clinician on a 7-point scale based on observation, parent report, and other records Yields cutoff scores, standard scores, and percentile ranks CARS-2 QPC. Unscored form: completed by parent or caregiver. These responses become the framework for follow-up interview information. Notes on ages:

-CARS-2-ST: 2 years to < 6 and those with communication difficulties or below average estimated IQs

-CARS-2-HF: +6years for verbally fluent individuals with IQ scores CARS-2-QPC: For parent or caregiver of an individual of any age.

-Factor pattern loadings from principal axis factor analysis with rotation of CARS items over 80.

The Stanford Binet Intelligence Scale, forth edition (SB4), : All participants underwent assessment by the arabic version **(Melika, 1998)** of Stanford– Binet test (fourth edition) (Delany& Hopkins, 1986) a standardized and well validated psychometric testing used to assess memory, attention, language, and concentration. Stanford–Binet test is formed of vocabulary, comprehension, verbal relations test, abstract visual reasoning test, quantitative reasoning test, memory for sentences test, bead memory test and intelligent quotient. This test is characterized by its acceptability to children, and relevance to daily livings activities in children group of population. ***(Delany& Hopkins, 1986)*** **,** 4th Edition. modified by ***(Melika, 1998).***

Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for ADHD: The diagnosis for Attention –Deficit Hyperactivity Disorder (ADHD) was based on strict DSM-IV criteria for ADHD (DSM-IV; American Psychiatric Association, 2000). The diagnostic information about the children was obtained through structured interviews with teachers and caregivers. The interviews included all symptoms related to ADHD. Each item scored yes if the symptom was

endorsed as definitely present or no if the respondent indicated either sometimes, rarely, or never. The diagnostic criteria used for final diagnosis and for classification of students with ADHD into its different subtypes (Hyperactive- impulsive, combined and inattentive types) ***(American Psychiatric Association, 2000)*** , modified by Prof. Soheir Kamil , faculty of Kindergartens, Cairo University, 2010 .

Socioeconomic scale *(Abdel-Tawab; 2010).*

It contains four main variables

1- The educational level of the father and mother.

2- The occupation of the father and mother.

3- Total family income.

4- Lifestyle of the family.

Each main variable involves a set of levels or branches, these levels are weighted on a graded scale starting with grade one and ended by a number corresponding to the rank of this level.

Each level has a score; the sum of these scores gives the total mark of the variable.

The total (row) score of an individual can be obtained from an equation that depends upon these four variables categorization of individuals of a given sample as high, middle, or low class is done as follow :

a- Calculation of the mean and SD for the total scores of the studied sample.

b- Individuals having score higher than mean + one SD are classified as high SES class.

c- Individuals having score lower than mean - one SD are classified as low SES class.

d- Individuals in between are classified as middle SES class (Abdel-Tawab; 2010).

Statistical analysis:

Data were analyzed using SPSS 26 (IBM SPSS Inc., Chicago, USA)) for windows. Categorical data were expressed as frequency and percent while quantitative data were expressed as minimum, maximum, mean, and standard deviation.

Results:

Our results will be demonstrated in the following tables:

Table (1): Demographic Data of Studied Autistic Children (N=20):

Demographic Data		F	%
Sex	Male Female	12 8	60% 40%
Age (years)	Mean+_SD Median (IQR)	1.5-15.0 7.43±3.23 7.0 (5-9.75)	-
Residence	Urban Rural	7 13	35% 65%
Social class	High Low	3 17	15% 85%
Maternal education	High Low	3 17	15% 85%
Advanced maternal age >35 years	Positive Negative	1 19	5% 95%
Advanced Paternal age>35 years	Positive Negative	1 19	5% 95%
Consanguinity	Positive Negative	9 11	45% 55%
Family history of ASD	Positive Negative	5 15	25% 75%

Continuous data expressed as mean ± SD and median (range).

Categorical data expressed as Number (%).

IQR: Inter Quartile Range SD: Standard deviation.

Table (1): Shows that 60% of the autistic children were males and 40% were females. 45% of parents were consanguineous. Family history of autism was 5%. Maternal age more than 35 years in 5% of children. the current study have shown that low socioeconomic status (85%) is significantly associated with ASD.

Table (2): Perinatal history of Studied Autistic Children (N=20):

Prenatal factors:		F	%
Preeclampsia	Positive Negative	0 20	0 100%
D.M	Positive Negative	0 20	0 100%
Drugs	Positive Negative	0 20	0 100%
Maternal infection	Positive Negative	0 20	0 100%
Maternal bleeding	Positive Negative	0 20	0 100%
Threatened abortion	Positive Negative	0 20	0 100%
Chemical radiation exposure	Positive Negative	0 20	0 100%

Natal factors:		**F**	**%**
Preterm	Full term	20	100%
	Post term	0	0
Delivery method	Vaginal	8	40%
	C.S	12	60%
Prolonged labor	Positive	1	5%
	Negative	19	95%
Hypoxia	Positive	2	10%
	Negative	18	90%
Ischemia, Trauma	Positive	0	0
	Negative	20	100%
Postnatal factors:		**F**	**%**
Resuscitations	Positive	1	5%
	Negative	19	95%
Neonatal jaundice	Positive	1	5%
	Negative	19	95%
Pallor	Positive	0	0
	Negative	20	100%
History of NICU admission	Positive	3	15%
	Negative	17	85%
Feeding	Bottle	10	50%
	Breast	10	50%

Table (2): Shows that 60% of cases delivery cesarean section, 5% prolonged labor, 5% needed positive resuscitations and 15% needed NICU admission. Feeding among children was artificial in 50% and breast-feeding in 50% of them.

Table (3) : Social Risk Factors of Studied Autistic Children (N=20):

Social Risk Factors		**F**	**%**
History of Exposure to Media (T.V , Mobile) more than Two Hours per Day	Positive	19	95%
	Negative	1	5%
Social Deprivation	Positive	15	75%
	Negative	5	25%
Delayed language Skills	Positive	20	100%
	Negative	0	0
Social Communication	Poor	18	90%
	Moderate	2	10%

Table (3): Shows that 95% of the cases have a positive history of exposure to media (television and mobile phone) for more than two hours daily at an early age, and 75% have a positive history of social deprivation, and all patients have a delay in language skills by 100% and 90% of our patients suffer from poor social communication.

Table (4): Clinical Characteristics of Studied Autistic Children (N=20):

	Clinical Characteristics		F	%
1	**Stereotyping movement**	Positive	18	90%
		Negative	2	10%
2	**Hyperactivity**	Positive	19	95%
		Negative	1	5%
3	**Hypo-activity**	Positive	1	5%
		Negative	19	95%

Table (4): Shows 90% of patients were positive for stereotyping movement, 95% are hyperactive but 5% hypoactive.

Table (5): Distribution of the studied autistic children according to Childhood Autism Rating Scale (CARS) (N=20):

Childhood Autism Rating Scale (CARS)	F	%
Mild to moderate autism (30-36.5)	11	55 %
Severe autism (37 to 60)	9	45%

Table (5): The patients were divided according to CARS into 11 patients (55%) with mild to moderate autism and 9 patients (45%) with severe autism.

Table (6): Classification of I.Q level of the studies autistic children according to the Stanford Binet intelligence scale (SB5) fifth edition (N=20):

I.Q level according to (SB5)	F	%
Mentally defective > 70	1	5%
Mild (55-69)	5	25%
Moderate (40-54)	8	40%
Severe > 35	6	30%

Table(6): IQ level of the studied autistic children according to (SB5) show that 25% had IQ scores in the average range, 24% were in the borderline range, and 5% in the mentally defective range.

Discussion:

Autistic spectrum disorder (ASD) is a group of neurodevelopmental disorders characterized by impaired social interaction and communication, repetitive and stereotyped behaviors, and restricted interests **(Lord et al., 2020).**

The current study included 20 patients (12 (60%) patients were males 8 (20%) patients were females) diagnosed as ASD, attending the neurology pediatric clinic of Al-Azhar university Hospital Assiut from 1st of November 2023 till 30th April 2024. Their ages ranges from 2 years to 12 years with mean ≤SD (7.43+3.23) years.

The majority of patients 13 (65%) came from rural areas. This agreed with the study done by **(CDC., 2023)** which found the majority of patients were males.

Current study have shown that low socioeconomic status (85%) is significantly associated with ASD, This agreed with many studies and disagree with others as reported by (**Thomas, 2011).** In following details ,Among the children with autism, younger age at diagnosis and a greater number of evaluations were also associated with higher SES. In a multistate study, the CDC ADDM network had previously reported an association of higher prevalence of autism with higher SES. (**Durkin, Maenner et al. 2010**). We suspect that having greater resources provides greater sensitivity in the diagnosis of autism, but there may be the possibility that an etiologic factor is also associated with both autism and SES.

In current study, positive family history of autism was 25% and 45% of parents were consanguineous. This was in agreement with **(Xie S, et al., 2019)** who concluded that family history of mental and neurological disorders is associated with ASD.

Also **(Chaste P, Leboyer M. (2012)** reported that family history of autism was present in 25% among patients group and consanguinity was detected in 45% Of them.

In current study, five percent of mothers aged more than 35 years. At birth of their autistic children. This was similar to **(Parner et al. 2012)** who find that advanced maternal age at birth was found in 23% of autistic children.

There's no History of prematurity in the study was present in cases, while all cases are full term birth. The type of feeding among children was artificial in (50%) and breast feeding in (50%) of them. This was in disagreement with **(Shawky et al., 2014)** who found that 10% of the patients have a history of prematurity, (65%) were breast fed and (35%) were artificially fed.

As regard to pregnancy complications, maternal infection no reported cases of mothers, no cases of maternal bleeding or pre-eclampsia and none of studied mothers reported history of chemical or radiation exposure during pregnancy.

A study by **(Bolton et al., 1992)** demonstrated an association between autism and obstetric complications, prenatal or intrapartum use of medications.

As regards to natal and postnatal factors, our study show high percent of cesarean delivery (60%), prolonged labour in (5%) of cases, (5%) of the studied children needed resuscitation after delivery, (15%) of them needed NICU admission. This is in agreement with many authors; **(El-Baz et al.,2011)** report that instrumental delivery was significantly higher among cases than controls and history of hypoxia, resuscitation, neonatal jaundice were also statistically significant. Also **(Kolevzon et al., 2007)**, suggested the presence of non-heritable prenatal, and perinatal risk factors for autism.

In current study, social milestones were significantly impaired among all autistic children, also stereotyped movements are present in all cases. This is in agreement with **(Juneja M, et al., 2005)** that reported about 96% of autistic children had motor developmental delay and qualitative impairment in social interaction and communication.

Some of the frequent comorbidities with autism include delayed speech and language skills, According to **(Tammimies K, 2019)** up to 30% of individuals with ASD ultimately do not acquire verbal speech.

Also some children with ASD will be reported to have a regression in previously acquired language, most typically between 18 and 24 months of age.

In current study, all included children have language impairment. This can be explained

that culturally, in Egypt parents tend to seek psychiatrist advice more when the child exhibits delayed speech.

Autism is a multifactorial disorder resulting from an interaction of genetic and environmental factors. Hundreds of autism risk genes and various environmental factors have been discovered **(Lord et al., 2020)**

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Conclusion:

From our study & results we concluded that risk factors of ASD associated with high incidence of autism among children. Severity of ASD symptoms and delay early diagnosis of autism in correlation with low socioeconomic level and low educational level of mothers. on other hand early avoidance of risk factors decrease incidence of ASD and early screening and diagnosis of autistic child decrease severity of symptoms and increase response for behavioral and social treatment.

Recommendation:

- Early diagnosis of ASD at a younger age allows for earlier behavioral and social interventions can dramatically improve outcomes for children on the spectrum and get good prognosis.
- Raising awareness about autism spectrum disorder and its risk factors especially early exposure to media like mobile phones and T.V and its hazards.
- Hoping more researches In the future include large numbers of autistic patients that would make the results more reliable.
- Follow CDC instructions about screen time limits and American Pediatric Association recommendations which is:
    - Do not utilize media viewing (TV, Video and DVD) and computers with children younger than 2 years.
    - Limit total media time for children 2 years and older to not more than 30 minutes weekly.
    - Use screen media with children ages 2 years and older only for educational purposes or physical activity.
    - Do not utilize TV, video or DVD viewing during meal or snack time.
    - APP recommends minimizing or eliminating media exposure, other than video chatting for children under the age of 18 months.

Limitations:

- The limitations of our study were the small sample size; the children were chosen from a single center and further investigation as molecular genetics and function MRI brain could not be done because the facility was not available in our hospital. A limited sample size included was some of the limitations of our study.
- **Declaration of conflicting interests:**

  The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this study.

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